

FIGURE 1

Human G Protein Coupled Receptor Family

(Receptors known as of January, 1999)

CLASS	LIGAND	NUMBER	TISSUE	PHYSIOLOGY	THERAPEUTICS
•Class I Rhodopsin like					
	•Amine				
	•Acetylcholine (muscarinic & nicotinic)	5	Brain, Nerves, Heart	Neurotransmitter	Acuity, Alzheimer's
	•Adrenoceptors				
	•Alpha Adrenoceptors	6	Brain, Kidney, Lung	Glucoregogenesis	Diabetes, Cardiovascular
	•Beta Adrenoceptors	3	Kidney, Heart	Muscle Contraction	Cardiovascular, Respiratory
	•Dopamine	5	Brain, Kidney, GI	Neurotransmitter	Cardiovascular, Parkinson's
	•Histamine	2	Vascular, Heart, Brain	Vascular Permeability	Anti-inflammatory, Ulcers
	•Serotonin (5-HT)	16	Most Tissues	Neurotransmitter	Depression, Insomnia, Analgesic
	•Peptide				
	•Angiotensin	2	Vascular, Liver, Kidney	Vasoconstriction	Cardiovascular, Endocrine
	•Bradykinin	1	Liver, Blood	Vasodilation,	Anti-inflammatory, Asthma
	•C5a anaphylatoxin	1	Blood	Immune System	Anti-inflammatory
	•Fmet-leu-phe	3	Blood	Chemoattractant	Anti-inflammatory
	•Interleukin-8	1	Blood	Chemoattractant	Anti-inflammatory
	•Chemokine	6	Blood	Chemoattractant	Anti-inflammatory
	•Orexin	2	Brain	Fat Metabolism	Obesity
	•Noctepin	1	Brain	Bronchodilator, Pain	Airway Diseases, Anesthetic
	•CCK (Gastrin)	2	Gastrointestinal	Motility, Fat Absorption	Gastrointestinal, Obesity, Parkinson's
	•Endothelin	2	Heart, Bronchus, Brain	Muscle Contraction	Cardiovascular, Respiratory
	•Melanocortin	5	Kidney, Brain	Metabolic Regulation	Anti-inflammatory, Analgesics
	•Neuropeptide Y	5	Nerves, Intestine, Blood	Neurotransmitter	Behavior, Memory, Cardiovascular
	•Neurotensin	1	Brain,	CNS	Cardiovascular, Analgesic
	•Opioid	3	Brain,	CNS	Depression, Analgesic
	•Somatostatin	5	Brain, Gastrointestinal	Neurotransmitter	Oncology, Alzheimer's
	•Tachykinin (Substance P, NKA ₁)	3	Brain Nerves	Neurohormone	Depression, Analgesic
	•Thrombin	3	Platelets, Blood Vessels	Coagulation	Anti-coagulant, Anti-inflammatory
	•Vasopressin-like	4	Arteries, Heart, Bladder	Water Balance	Anti-diuretic, Diabetic Complications
	•Galanin	1	Brain, Pancreas	Neurotransmitter	Analgesics, Alzheimer's
	•Hormone protein				
	•Follicle stimulating hormone	1	Ovary, Testis	Endocrine	Fertility
	•Lutropin-choriogonadotropic	1	Ovary, Testis	Endocrine	Fertility

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•Thyrotropin	1	Thyroid	Endocrine	Thyroidism, Metabolism
•Rhodopsin	5	Eye	Photoreception	Ophthalmic Diseases
•Opsin	4 (~1000)	Nose	Smell	Olfactory Diseases
•Olfactory				
•Prostanoid	5	Arterial, Gastrointestinal	Vasodilation, Pain	Cardiovascular, Analgesic
•Prostaglandin	2	Vessels, Heart, Lung	Inflammation	Cancer, Anti-Inflammatory
•L-lysophosphatidic Acid	2	Most Cells	Cell proliferation	Cancer
•Sphingosine-1-phosphate	1	White Blood Cells, Bronchus	Inflammation	Asthma, Rheumatoid Arthritis
•Leukotriene	1	Arterial, Gastrointestinal	Platelet Regulation	Cardiovascular
•Prostacyclin	1	Arterial, Bronchus	Vasoconstriction	Cardiovascular, Respiratory
•Thromboxane	1			
•Nucleotide-like	4	Vascular, Bronchus	Multiple Effects	Cardiovascular, Respiratory
•Adenosine	4	Vascular, Platelets	Relaxes Muscle	Cardiovascular, Respiratory
•Purinceptors	2	Brain	Sensory Perception	Analgesics, Memory
•Cannabinoids	1	Most Peripheral Tissues	Inflammation	Anti-inflammatory, Anti-asthmatic
•Platelet activating factor				
•Gonadotropin-releasing hormone like				
•Gonadotropin-releasing hormone	1	Reproductive Organs, Pituitary	Reproduction	Prostate Cancer, Endometriosis
•Thyrotropin-releasing hormone	1	Pituitary, Brain	Thyroid Regulation	Metabolic Regulation
•Growth hormone-inhibiting factor	1	Gastrointestinal	Neuroendocrine	Oncology, Alzheimer's
•Melatonin	1	Brain, Eye, Pituitary	Neuroendocrine	Regulation of Circadian Cycle
•Secretin	1	Gastrointestinal, Heart	Digestion	Obesity, Gastrointestinal
•Calcitonin	1	Bone, Brain	Calcium Resorption	Osteoporosis
•Corticotropin releasing factor/urocortin	1	Adrenal, Vascular, Brain	Neuroendocrine	Stress, Mood, Obesity
•Gastric inhibitory peptide (GIP)	1	Adrenals, Fat Cells	Sugar/Fat Metabolism	Diabetes, Obesity
•Glucagon	1	Liver, Fat Cells, Heart	Gluconeogenesis	Cardiovascular
•Glucagon-like Peptide 1 (GLP-1)	1	Pancreas, Stomach, Lung	Pancreas, Stomach, Lung	Cardiovascular, Diabetes, Obesity
•Growth hormone-releasing hormone	1	Brain	Neuroendocrine	Growth Regulation
•Parathyroid hormone	1	Bone, Kidney	Calcium Regulation	Osteoporosis
•PACAP	1	Brain, Pancreas, Adrenals	Metabolism	Metabolic Regulation
•Vasoactive intestinal polypeptide (VIP)	1	Gastrointestinal	Motility	Gastrointestinal
•Metabotropic Glutamate	7	Brain	Sensory Perception	Hearing, Vision
•GABA _A	1	Brain	Neurotransmitter	Mood Disorders
•Extracellular Calcium Sensing	1	Parathyroid, Kidney, GI Tract	Calcium Regulation	Cataracts, GI Tumors

•Class II
Secretin like

•Class III

Figure 2

G protein-coupled receptors:

(Division into Class A

Or Class B)

1. **A1 adenosine receptor** [Homo sapiens]. ACCESSION AAB25533
npivyaf riqkfrvtfl kiwndhfcq pappidedlp eerpdd
Class A
2. **adrenergic, alpha -1B-, receptor** [Homo sapiens]. ACCESSION NP_000670
npiiyccskefkrafvrlgcqgrgrmmrrmlggcaytrpwtgrgslersqrkdslddsgscslsgqrtlpsaspspgylgrgag
ppvelcaspewkapgallslpapeppgrrrghdsgplftfkdltepespgtdggasnggceaaadvangqpgfksnmplapggf
Class A
3. **adrenergic receptor alpha-2A** [Homo sapiens]. ACCESSION AAG00447
npviytfihhdffrafkilcrgrdkriv
Class A
4. **alpha-2B-adrenergic receptor** - human. ACCESSION A37223
npviytfifnqdfrafrilcrpwqtaw
Class A
5. **alpha-2C-adrenergic receptor** - human. ACCESSION A31237
npviytfvfnqdfirpsfkhlfrmrgrfrq
Class A
6. **beta-1-adrenergic receptor** [Homo sapiens]. ACCESSION NP_000675
npiiycrpsdfrikaqfllccarraarrhathgdrprasglarpgpppsgaasdddddvgatpparllcpwagcngaaads
d ssldepcrpgfaseskv
Class A
7. **beta-2 adrenergic receptor**. ACCESSION P07550
npliycrpsdfrikaqfllclrrsslkayngyssngntgeqsgyhyveqekenklcedlpgtdfvgghqgtvpsdnidsqgrmcstnd
sll
Class A
8. **dopamine receptor D1** [Homo sapiens]. ACCESSION NP_000785
npiiyafnadrfkafstllgcyrllcpatnnaietvsinnngaamfsshheprgsiskecnlyliphavgssedlkkeeaagiarplekls
palsvildytdvslckiqpitqngqhpt
Class A
9. **D(2) dopamine receptor**. ACCESSION P14416
npiiyttfniefkafllkilhc
Class A
10. **d3 dopamine receptor** - human. ACCESSION G01977

npviyttfniefkafkilscl
Class A

11. **dopamine receptor D4** - human. ACCESSION DYHUD4
npviytfvnaefrnvfrkalracc
Class A

12. **dopamine receptor D5** - human. ACCESSION DYHUD5
npviyafnadfqkvfaqllgcshfcsrtptvetvnisnelisynqdivfhkeiaaayihmmpnavtpgnrevndeeegpfdrmfqi
yqtspdgdpvaesvwelcdcegeisldkitpftpngfh
Class A

13. **muscarinic acetylcholine receptor M1** [Homo sapiens]. ACCESSION NP_000729
nmpcyalcnafrtdfrlllcrwdkrrwrkipkrpgsvhrtpsrqc
Class A

14. **muscarinic acetylcholine receptor M2** [Homo sapiens]. ACCESSION NP_000730
npacyalcnatfkkfthllmchyknigatr
Class A

15. **muscarinic acetylcholine receptor M3** [Homo sapiens].
npvcyalcnktftrtkmlllcqedkkrkqqyqqrqsvifhkrpeqal
Class A

16. **muscarinic acetylcholine receptor M4** [Homo sapiens]. ACCESSION NP_000732
npacyalcnatfkkftrhlllcqymrigtar
Class A

17. **m5 muscarinic receptor**. locus HUMACHRM ACCESSION AAA51569
npicyalcnrtrfktfkmlllcrwkdkkveeklywqgnsklp
Class A

18. **5-hydroxytryptamine (serotonin) receptor 1A** [Homo sapiens]. ACCESSION BAA90449
npviyayfnkdfqnafkkiikckf
Class A

19. **5-hydroxytryptamine (serotonin) receptor 1B** [Homo sapiens]. ACCESSION BAA94455
npiiytmsnedfkqafhklirfckts
Class A

20. **5-hydroxytryptamine (serotonin) receptor 1E** [Homo sapiens]. ACCESSION BAA94458
npilytsfnedfklaflkklirere
Class A

21. **OLFACTORY RECEPTOR 6A1**. ACCESSION O95222

Figure 2
 page 3

npiiyclnqevkralccihlyqhqdppkkgsmv

Class A

22. OLFACTORY RECEPTOR 2C1. ACCESSION O95371

npliytlnmmevkgafrlllgkgrevg

Class A

23. angiotensin receptor 1 [Homo sapiens]. ACCESSION NP_033611

npflfygflgkfkryflqllykypkakshsnlsfkmstfsyrpsdnvsssttkpapcfve

Class B

24. angiotensin receptor 2 [Homo sapiens]. ACCESSION NP_000677

npflfygfnrnfqqklrsvfrvptwlqgkresmscrkssslremetfvs

Class B

25. interleukin 8 receptor beta (CXCR2) [Homo sapiens]. ACCESSION NM_001557

NPLIYAFIGQKFRHGLLKILAIHGLISKDSLPKDSRPSFVGSSSGHTSTTL

Class B

26. cx3c chemokine receptor 1 (cx3cr1) (fractalkine receptor)

ACCESSION P49238

npliyafagekfrrylyhlygkclavlgrsvhvdssscsqsrshgsvlsnftyhtsgdallll

Class B

27. neurotensin receptor - human. ACCESSION S29506

n pilynlvsanfrhiflatlaclcpvwrtrrkpafsrkadsvssnhfssnatretly

Class B

28. SUBSTANCE-P RECEPTOR (SPR) (NK-1 RECEPTOR) (NK-1R). ACCESSION P25103

npiiycolndrflgfkhafrccpfisagdyeglemkstrylqtqsgvykvsrletftstfvgahecepedgpkatpssldltnccssrsd
 sktmtesfsfsnvlsl

Class B

29. vasopressin receptor type 2 [Homo sapiens]. ACCESSION AAD16444

npwiyasfsssvsselsrllccargtrppslgpdcsctassslakdtss

Class B

30. thyrotropin-releasing hormone receptor - human. ACCESSION JN0708

npviynlmsqkfrraafkclonckqkptekpanyvalnsvikesdhfsteldditvtdtlylsafkvsfddclasevvsfsqs

Class B

31. oxytocin receptor - human. ACCESSION A55493

npwiymlftghlhelvqrfccsasyllgrrlgetsaskksnsssfvlsrshsssqrsccqpsta

Class B

32. **neuromedin U receptor 1 [Homo sapiens]**. ACCESSION AAG24793
npvlyslmssrfretfqealcigacchrlprhsshslsrmmtgtclcdvsglsgwvhplagndgpeaqgetdps
Class B
33. **gastrin receptor**. ACCESSION AAC37528
nplvycfmhrrfrqacletcarceprpprarpralpdedpptpsiaslsrlsyttistlpgg
Class B
34. **galanin receptor 3 [Homo sapiens]**. ACCESSION 10879541
nplvyalasrhfrfirlwpcgrrrrhramalrrvpasggppgcpgdarpsgrllaggqgqpepregpvhggeaargpe
Class A
35. **edg-1 - human**. ACCESSION A35300
npiiytltnkemrrafirmsockcpsgdsagkfkrrpiagmefsrksksdnsshpqkdegdnpetimssgnvnss
Class A
36. **central cannabinoid receptor [Homo sapiens]**. ACCESSION NP_057167
npiiyalrskdlrhafismfpcsgtaqpldnsmgdsdclhkhannaasvhraaescikstvkiakvtmstvstdtsacal
Class A
37. **delta opioid receptor - human**. ACCESSION I38532
npvlyafldenfkrfqlrkpcgrdpssfsrpreatarervtactpsdggpgggraa
Class A
38. **proteinase activated receptor 2 (PAR-2) human**. ACCESSION P55085
dpfvlyvfshdfrdhaknallcrsvrtvkqmqvsltskkhsrkssysststvtksy
Class B
39. **vasopressive intestinal peptide receptor (VIPR) rat**. ACCESSION NM_012685
NGEVQAEFLRRKWRRWHLQGVLGWSSKSQHPWGGSGNGATCSTQVSMLTRVSPSARR
SSSFQAEVSLV
Class B

Figure 3

A. Human V2R DNA (nucleotides encoding the last 29 amino acids of the V2R and the adjacent stop codon):

gcccgggggacgcacccccaccagcctgggtccccaagatgagtctctgcaccacgccagctctc
cctggccaaggacattcatcgtga

B. PCR amplified human V2R DNA fragment:

gcggccgcacggggacgcacccccaccagcctgggtccccaagatgagtctctgcaccacgcc
agctctcctcctggccaaggacattcatcgtgaagatctccgcggtctaga

*Additions and changes to the V2R DNA are underlined.

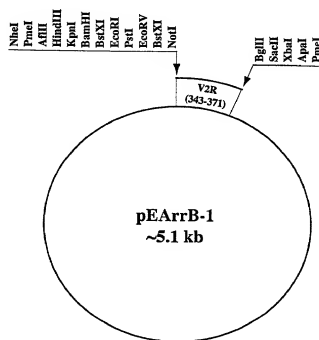
*The Sma I (cccgga) restriction enzyme site (underlined in Fig. 3A) was eliminated in the amplified DNA fragment by changing a cytosine to an adenine.

*A Not I restriction site (gcggccgc) was incorporated into the amplified DNA fragment by adding 6 nucleotides (gcggcc) to the 5' end of the V2R DNA.

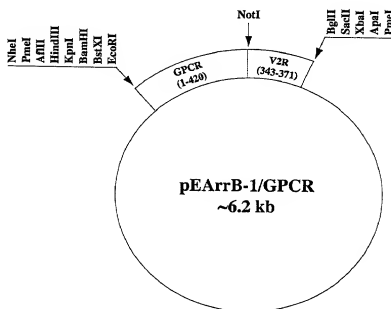
*Bgl II (agatct), Sac II (ccggga), and Xba I (tctaga) restriction enzyme sites were added to the 3' end of the V2R DNA.

Figure 4

A.



B.



C.

...AAARGRTTPPSLGPQDESCTTASSSLAKDTSS

Figure 5

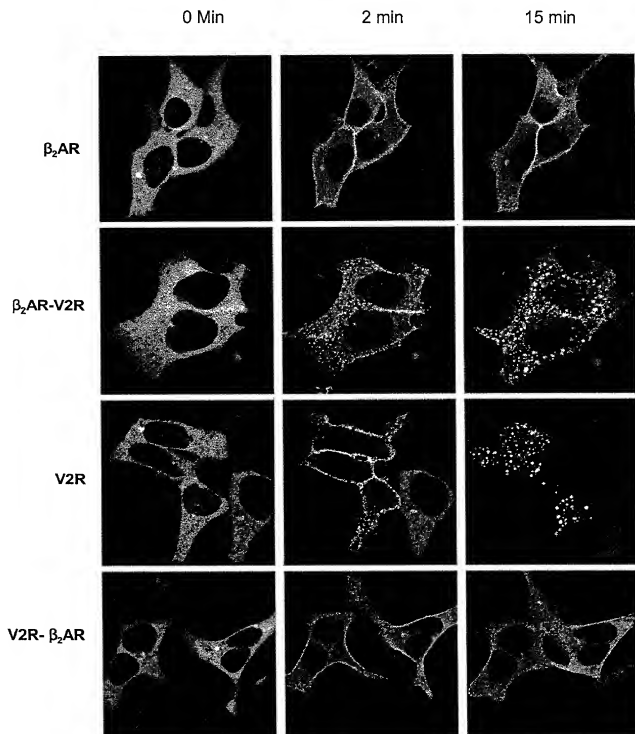


Figure 6

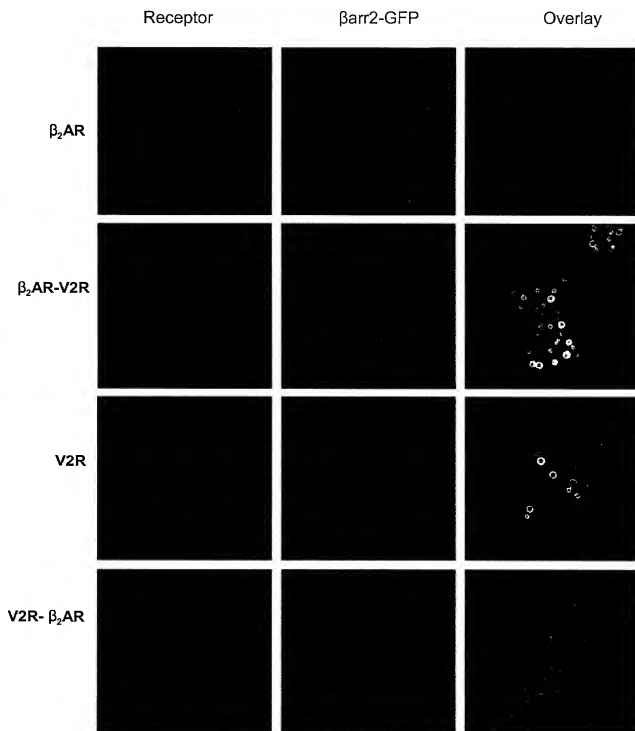


Figure 7

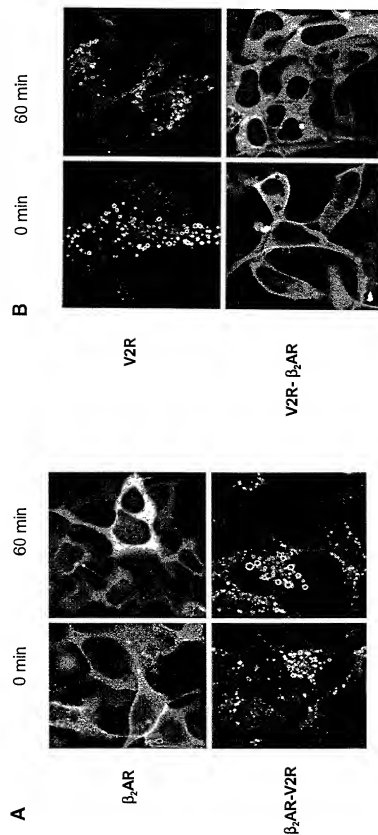


Figure 8

A

- 1) V2R CARGRTPPSLGPQDESCCTTASSSLAKDTSS
 2) V2R-S362X CARGRTPPSLGPQDESCCTTA
 3) V2R-SSSTSS/AAAAAA CARGRTPPSLGPQDESCCTTAAAAAKDAAA
 4) V2R-TSS/AAA CARGRTPPSLGPQDESCCTTAAAAAKDAAA
 5) V24-SSS/AAA CARGRTPPSLGPQDESCCTTAAAAAKDTS
 6) β_2 AR-V2R-SSS/AAA CARGRTPPSLGPQDESCCTTAAAAAKDTS
 7) β_2 AR CLRSSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP-
 GTEDFVGHQGTVPDNDISQGRNCSTNDSL
 8) β_2 AR413-V2R10 CLRSSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP-
 GTEDFVGHQGTVPDNDISQGRNCSTNDSLSSSLAKDTSS
 9) B2ar360-V2R10 CLRSSSLKAYGNGYSSNGNTSSSLAKDTSS

B

V2R NPWIIASFSSSVSELRSLLCCARGRTPPSLGPQDESCCTTASSSLAKDTSS
 AAA-1 -----AAA-----
 AAA-2 -----AAA-----
 NTR-1 NPILYNLVANFRQVFLSTLACLCPGWRHRRKKRPTFSRKPNMSMSSNHAFSTSATRETRY
 AMAA -----A-AA-----
 AAA -----AAA-----
 OTR NPWIIYMLFTGHLFHELVRFLCCSASYLKGRRLGETSASKKSNSSSFVLSHRSSQRSCSQPSTA
 AAAA -----AAAA-----
 AAA-1 -----AAA-----
 AAA-2 -----AAA-----

C

SPR NPIIYCCLNDRFRLGFKHAFRCPPFISAGDYEGLEMKSTRYLQTQGVYKVSRLTITITIVVGAHEEEPE-
 GPKATPSSKLTSNCSSRSDSKTMTESFSFSSNVLS
 383X -----X
 355X -----X
 325X -----X
 AAIAA -----AA-AA-----
 AAA -----A-AA-----

Figure 9

Amino Acid Sequence of the Wild-Type Receptors

A. Amino acid sequence of the wild-type V2R

MLMASTTSAPVPGHPSLPSLPSNSSQERPLDTRDPLLARAEIALLSIVFVAVAL
SNGLVLAALARRGRRGHWAPIHVFIGHLCLADLAVLQVLPQLAWKATDRFR
GPDALCRAVKYLQVMGYASSYMLAMTLDRHRAICRPMLAYRHGSGAHWNRP
VLVAVAFSLLLSLPQLFIFAQRNVEGGSGVTDCWACFAEPWGRRTYVTTWIALM
VVFAPTGLGIAACQVLIFREIHASLVPGPSPERPGRRRGRRTGSPGEGAHVSAA
VAKTVRMTLVIVVVVVLWCWAPFFLVQLWAAWDPEAPLEGAPFVLLMLLASLNS
CTNPWIIYASFSSSSSELRSLLCC**ARGRTPPSLGPQDESCTTASSSLAKDTSS**
(Seq. ID No. 1)

B. Amino acid sequence of the wild-type β 2AR

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMGIVMSLIVLAIVFGNVL
VITAIKFERLQTVTNYFITSLACADLMGLAVVPFGAAHILMKMWTFGNFWC
EFWTSIDVLCVTASIEITLCVIAVDYFAITSPFKYQSLLTKNKARVILMVWI
VSGLSFLPIQMHWRATHQEAENCYANETCCDFFTNQAYAIASSIVSFYVPL
VIMVFVYSRVFQEAQRQLQKIDKSEGRFHVQNLSQVEQDGRTHGLRRSSKFC
LKEHKALKTLGIIMGTFTLCWLPPFFIVNIVHVIQDNLIRKEVYILLNWIGYVN
SGFNPLIYCRSPDFRIAFQELLCLRRSSLKAYGNGYSSNGNTGEQSGYHVEQE
KENKLLCEDLPGTEDFVGHQGTVPSPDNIDSQGRNCSTNDSLL
(Seq. ID No. 2)

Amino Acid Sequence of the Chimeric Receptors

C. Amino acid sequence of the β 2AR-V2R chimera (Oakley et al.)

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMGIVMSLIVLAIVFGNVL
VITAIKFERLQTVTNYFITSLACADLMGLAVVPFGAAHILMKMWTFGNFWC
EFWTSIDVLCVTASIEITLCVIAVDYFAITSPFKYQSLLTKNKARVILMVWI
VSGLSFLPIQMHWRATHQEAENCYANETCCDFFTNQAYAIASSIVSFYVPL
VIMVFVYSRVFQEAQRQLQKIDKSEGRFHVQNLSQVEQDGRTHGLRRSSKFC
LKEHKALKTLGIIMGTFTLCWLPPFFIVNIVHVIQDNLIRKEVYILLNWIGYVN
SGFNPLIYCRSPDFRIAFQELL**CARGRTPPSLGPQDESCTTASSSLAKDTSS**
(Seq. ID No. 3)

*shown in bold are the amino acids that were moved to the b2AR to increase its affinity for arrestin.

Figure 10

A. Amino acid sequence of the MOR-V2R chimera expressed from the pEArrB-1/MOR vector

MDSSTGPGNTSDCSDPLAQASCSPAGSWLNLSHVDGNQSDPCGLNRTGLGGN
DSLCPQTGSPSMVTAITIMALYSIVCVVGLFGNLFVMYVIVRYTKMTATNIY
IFNLALADALATSTLPFQSVNYLMGTWPFGTILCKIVISIDYYNMFTSIFTLC
TMSVDVRYIAVCHPVKALDFRTPRNAKIVNVCNWILSSAIGLPVMFMATTKYRQ
GSIDCTLTFSHPTWYWENLLKICVFIFAFIMPILIIITVCYGLMILRLKSVRML
SGSKEKDRNLRRITRMVLVVAVFIVCWTPIHIVIKALITIPETTFQTVSW
HFCIALGYNTSCLNPVLYAFLDENFKRCFREFCAAARGRTPPSLGPQDESCCT
ASSSLAKDTSS

(Seq. ID No. 4)

B. Amino acid sequence of the D1AR-V2R chimera expressed from the pEArrB-1/D1AR vector

MAPNTSTMDEAGLPAERDFSFRILTACFLSLLILSTLLGNTLVCAAVIRFRLH
RSKVTNFFVISLAVSDLLVAVLVMPWKAVAEIAGFWPFGSFCNIWVAFDIMCS
TASILNLCVISVDRYWAISSPFQYERKMTPKAAFILISVAVTSLVLISFIPVQ
LSWHKAKPTWPLDGNFTSLEDTEDDNCDTRLRSRTYAISSSLISFYIPVAIMIV
TYTSIYRIAQKQIRRIISALERAABVHAKNCQTTAGNGNPVECAQSESSFKMSFK
RETKVLKTLVIMGVFVCCWLPEFFISNCMVFPFCGSEETQPFCDISITFDVFVW
FGWANSSLNPIIYAFNADFQKAFSTLLGCYRLCAAARGRTPPSLGPQDESCCT
ASSSLAKDTSS

(Seq. ID No. 5)

C. Amino acid sequence of the 5HT1AR-V2R chimera expressed from the pEArrB-1/5HT1AR vector

MDVLSPGQGNNNTSPAPPFETGGNTTGISDVTVSQVITSLLLGLTIFCAVLG
NACVVAAIALERSLQNVANYLIGSLAVTDLMSVSLVLPMAALYQVNLKWTLGQ
VTCDLFIALDVLCTSSILHLCAIALDRYWAITDPIDYVNKRTPRRAALISL
TWLIGFLISIPMLGWRTPEDRSDPDCTISKDHGYTIYSTFGAFYIPLLLML
VLYGRIFRAARFRIRKTVKKVEKTGADTRHGASAPAPQPKSVNGESGSRNWRL
GVESKAGGALCANGAVRQDDGAALVIEVHRVGNKSKEHLPLPSEAGPTPCAP
ASFERKERNNAEAKRKMALEARERKTVKTLGIIMGTFILCWLPEFFIVALVLPFC
ESSCHMPTLLGAI

Figure 10 (cont.)

INWLGYSNSLLNPVIYAYFNKDFQNAFKKI IKCNFCAAARGRTPPSLGPQDES
CTTASSSLAKDTSS

(Seq. ID No. 6)

D. Amino acid sequence of the β 3AR-V2R chimera expressed from the pEArrB-1/ β 3AR vector

MAPWPHENSSLAPWPDLPPTLAPNTANTSGLPGVPWEAALAGALLALAVLATVG
GNLLVIVAIAWTPRLQTMTNVFVTSLAAADLVMGLLVVPPAATLALTGHWPVG
ATGCELWTSVDVLCVTASIELTLCALAVDRYLAVTNPLRYGALVTKRCARTAVV
LVVVVSAAVSFAPIMSQWVRVGADAEARQCHSNPRCCAFASNMPYVLLSSSVS
FYLPLLVMFLVYARVFVAVTRQLRLLRGELGRFPPEESPPAPSRSLAPAPVGT
CAPPEGVPACGRRPARLLPLREHRALCTGLGIMGTFTLCWLPFFLANVLRALG
GPSLVPGPAFLALNWLGYANSFNPILIYCRSPDFRSFAFRLLCRCAAARGRTP
PSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 7)

E. Amino acid sequence of the Edg1R-V2R chimera expressed from the pEArrB-1/Edg1R vector

MGPTSVPLVKHAHRSSVSDYVNYDIIVRHYNITGKLNISADKENSIKLTSVVF
LICCFIILENIFVLLTIWKTCKFHRPMYYFIGNLALSDLLAGVAYTANLLLSG
ATTYKLTPAQWFLREGSMFVALSASVFSLLAIAIERIYITMLKMKLHNGSNNFR
LFLLSACWVISLILGGLPIMGWNCISALSSCSTVLPYHKHYILFCTTVFTL
LLLSIVILYCRIYSLVRTRSRLTFRKNISKASRSEKSLALLKTVIIVLSVF
IACWAPLFILLLLDVGCKVKTCDILFRAEYFLVLAVLNSGTNPILIYTLTNKEM
RRAFIRIMSCCKCAAARGRTPPSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 8)

Figure 11

A. Nucleotide sequence of the β 2AR-V2R chimera

atggggcaaccggggaacggcagcgccctcttgctggcaccacatagaagccatgcgcgggacc
 acgacgtcacgcagcaaaaggagcaggtgtgggtggggcatgggcatcgatcatctctcat
 cgtcctggccatcgtgtttggcaatgtgctgggtcatcacagccattggcaagtccagcgtctg
 cagacggtcaccacactacttcatcacttcactggcctgtgctgatctggctcatgggcctggcag
 tgggtgcccccttggggcgcccatatcttatgaaaaatgtggacttttggcaactctgtgtgcga
 gtttgggacttccattgatgtgctgtgctgcacggccagcattgagaccctgtgcgtgatcgca
 gtggatcgctactcttgcattacttccaccttcaagtaccagagcctgtgacccaagaataagg
 cccgggtgatcattctgaggtgtggatgtgtgcaggccttacctcctcttgcgcattcagat
 gcaactggtacggggccaccaccagggaagccatcaactgctatgccaatgagacctcgtgtgac
 ttcttcacgaaccacagctatgccattgcctctccatcgtgtccttctacgttccccctggtga
 tcatggtctctgctctactccagggtcttctcaggaggccaaaaggcagctccagaagattgacaa
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B. Nucleotide sequence of the MOR-V2R chimera

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C. Nucleotide sequence of the D1AR-V2R chimera

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(SEQ ID No. 11)

D. Nucleotide sequence of the 5HT1AR-V2R chimera

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(SEQ ID No. 12)

E. Nucleotide sequence of the β 3AR-V2R chimera

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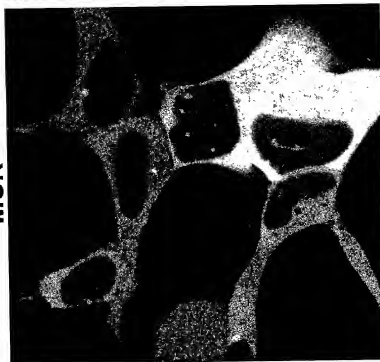
F. Nucleotide sequence of the Edg1-V2R chimera

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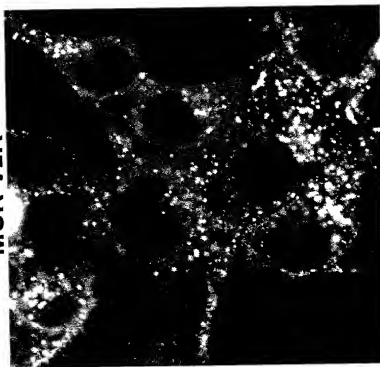
FIGURE 12

β arr2-GFP Translocation to the MOR and MOR-V2R Chimera
in Response to Morphine

MOR

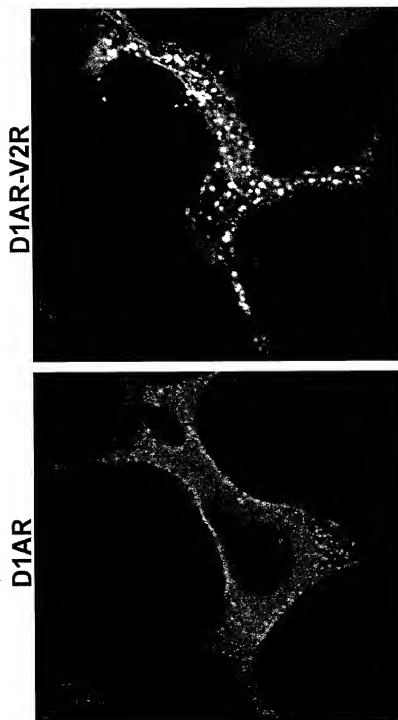


MOR-V2R



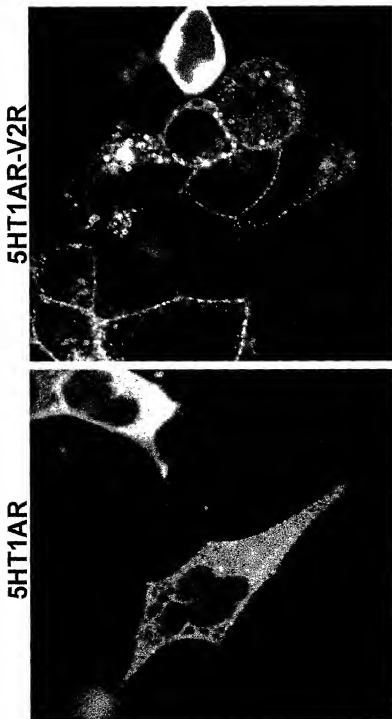
**β arr2-GFP Translocation to the D1AR and D1AR-V2R Chimera
in Response to Dopamine**

FIGURE 13



**β arr2-GFP Translocation to the 5HT1AR and 5HT1AR-V2R
Chimera in Response to Serotonin**

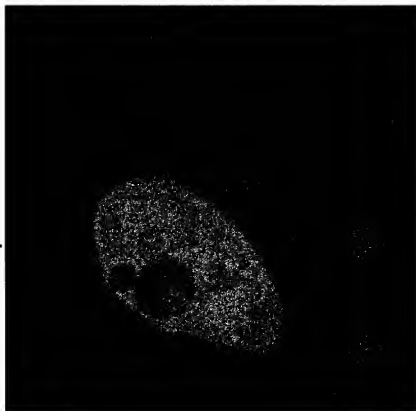
FIGURE 14



β arr2-GFP Translocation to the β 3AR and β 3AR-V2R Chimera in Response to Isoproterenol

FIGURE 15

β 3AR



β 3AR-V2R

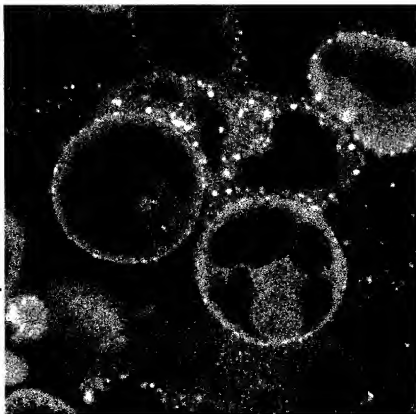


FIGURE 16

FIGURE 16

**β arr2-GFP Translocation to the Edg1 and Edg1-V2R Chimera
in Response to Spingosine-1-Phosphate**

